Please replace the paragraph beginning on page 5, line 15 with the following rewritten paragraph:

--The carboxy-terminus of human RNase H1 (SEQ ID NO:3) is highly conserved with *E. coli* RNase H1 (SEQ ID NO:1) and contains the amino acid residues of the putative catalytic site and basic substrate-binding domain of the *E. coli* RNase enzyme. The amino-terminus of human RNase H1 contains a structure consistent with a double-strand RNA (dsRNA) binding motif that is separated from the conserved *E. coli* RNase H1 region of the carboxy-terminus by a 62 amino acid sequence. We have performed site-directed mutagenesis on human RNase H1. These studies showed that although the conserved amino acid residues of the putative catalytic site and basic substrate-binding domain are required for RNase H activity, deletion of either the catalytic site or the basic substrate-binding domain did not ablate binding to the heteroduplex ~~sustrate~~ substrate. Deletion of the region between the dsRNA-binding domain and the conserved *E. coli* RNase H1 domain resulted in a significant loss in the RNase H activity. Furthermore, this deletion mutant competitively inhibited the cleavage activity of the wild-type enzyme suggesting that this central 62 amino acid region does not contribute significantly to the binding affinity of the enzyme for the substrate. The dsRNA-binding domain was not required for RNase

H activity, as the dsRNA-deletion mutants exhibited cleavage rates comparable to the rate observed for wild-type enzyme. Comparison of the dissociation constant of human RNase H1 and the RNase H1[ΔI-II] mutant for the heteroduplex substrate suggested that the greatest contribution to binding is from the region situated within the conserved *E. coli* RNase H1 region of human RNase H1. Finally, comparison of the cleavage patterns exhibited by the mutant proteins with the cleavage pattern for the wild-type enzyme indicates that the dsRNA-binding domain is responsible for the observed strong positional preference for cleavage exhibited by human RNase H1.--

Please replace the paragraph beginning on page 7, line 2 with the following rewritten paragraph:

--Figure 1. Schematic showing the structure of the human RNase H1 mutant proteins (SEQ ID NO:3). (A) Position of amino acid substitution mutants. Mutants include: asparagine substitution of aspartic acid at position 145 [D145N], glutamine substitution of glutamic acid at position 186 [E186Q], asparagine substitution of Aspartic acid at position 210 [D210N], alanine substitution of lysine at positions 226 and 227 [K226,227A] and alanine substitution of lysine at positions 226, 227, 231 and 236

[K226,227,231,236A]. The amino acids of regions I, II and II are represented by, respectively, in bold, underlined and plain lettering. Designations within parentheses indicate amino acid positions of *E. coli* RNase H1. (B) Description of deletion mutants of human RNase H1. RNase H1[ΔI] corresponds to the deletion of region I (amino acid positions 1 - 73), RNase H1[ΔII] corresponds to the deletion of region II (amino acid positions 74 - 135) and RNase H1[ΔI-II] corresponds to the deletion of regions I and II (amino acid positions 1 - 135).--

Please replace the paragraph beginning on page 8, line 6 with the following rewritten paragraph:

--**Figure 3. RNase H Cleavage site for wild-type and mutant proteins on the 17-mer RNA-DNA heteroduplex.** Digestion of the heteroduplex was preformed as described in Materials and Methods. The RNA sequence (5' → 3') (SEQ ID NO:2) is shown above the DNA sequence (SEQ ID NO:4). The arrows indicate the sites of enzymatic digestion, and the size of the arrows reflect the relative cleavage intensities. (A) Cleavage pattern for wild-type RNase H1, RNase H1[ΔII] and RNase H1[K226,227A] proteins. (B) Cleavage pattern for RNase H1[ΔI] and [ΔI-II] mutants.--